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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/818,954	03/27/2001	Christopher J.R. Paszty	A-676B	9125

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AMGEN INCORPORATED
MAIL STOP 27-4-A
ONE AMGEN CENTER DRIVE
THOUSAND OAKS, CA 91320-1799

EXAMINER
SPECTOR, LORRAINE

ART UNIT	PAPER NUMBER
1647	13

DATE MAILED: 07/11/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Offic
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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO.

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ART UNIT	PAPER NUMBER
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DATE MAILED:

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☒ Responsive to communication(s) filed on 5/21/03

☒ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1-8, 10, 11, 47-51, 61, 65 is/are pending in the application.
Of the above, claim(s) _____ is/are withdrawn from consideration.
☐ Claim(s) _____ is/are allowed.
☒ Claim(s) 1-8, 10, 11, 47-51, 61, 65 is/are rejected.
☐ Claim(s) _____ is/are objected to.
☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
☐ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.
☐ received in Application No. (Series Code/Serial Number) _____.
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of Reference Cited, PTO-892
☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____
☐ Interview Summary, PTO-413
☐ Notice of Draftperson's Patent Drawing Review, PTO-948
☐ Notice of Informal Patent Application, PTO-152

--SEE OFFICE ACTION ON THE FOLLOWING PAGES--

Part III: Detailed Office Action

The objection to claims 50 and 51 has been overcome by applicants amendments to the claims.

The objection to improper incorporation of essential material by reference to a WO publication has been overcome by applicants amendment.

The new title of the invention is acknowledged.

The double patenting rejections are moot as application 09/723970 is abandoned.

Objections and Rejections under 35 U.S.C. §101 and 112:

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-8, 10, 11, 47-51, 61 and 65 remain rejected under 35 U.S.C. § 101 because the claimed invention is not supported by either a specific, substantial and credible asserted utility or a well established utility for reasons of record in the previous Office Action, paper number 11 at pages 5-7.

Applicants traversal of this rejection in paper number 12 received 5/21/03 has been fully considered but is not deemed persuasive. At page 9, applicants argue that the disclosed β10 protein is a member of the cysteine knot growth factor structural superfamily. The Examiner has not questioned this designation. However, the cysteine know growth factor structural superfamily contains protein of many and varied functions; merely identifying a protein as belonging to such does not establish utility.

At pages 9-10 applicants argue that the transgenic experiment which shows that over expression of both β10 and α2 in the 'circulation' of transgenic mice caused thyroid enlargement,

multiple follicular papillary adenoma and hyperthyroidism establishes utility for the claimed invention. This argument has been fully considered but is not deemed persuasive because while these truly are not insignificant conditions, the Examiner does not find any nexus between the ability to cause such by overexpression of the claimed nucleic acids and utility. Applicants have not disclosed that the causation of thyroid enlargement, multiple follicular papillary adenoma and hyperthyroidism constitutes a useful model system for the study of disease, nor have they disclosed that these conditions are caused by overexpression of β10 *in vivo*. While it is certainly possible that it will be found in the future that β10 can be a cause of such conditions, the person of ordinary skill in the art would not accept such an assertion based upon the data presented in the specification as originally filed. As stated in the previous Office Action, being able to induce a condition by artificial overexpression of a DNA does not constitute a substantial showing that such overexpression actually occurs *in vivo*, nor what the 'normal' biological role of the encoded protein is. Thus, it remains that applicants suppositions as to clinical uses of the claimed DNA at the paragraph bridging pages 9-10 and the first full paragraph of page 10 of the response are merely speculative, and constitute an invitation to experiment to find such diseases or conditions, and then use the claimed DNA to treat such. Such experimentation constitutes part of the invention. Such utilities, if they actually exist, are not yet in available form, as no conditions or diseases have actually been associated with β10 expression.

Arguments pertaining to whether or not β10 and α2 dimerize in vivo are not on point. The issue here is that it is not clear that the ability to cause thyroid enlargement, multiple follicular papillary adenoma and hyperthyroidism in transgenic mice does not constitute a specific, substantial and credible, readily available utility, but merely is a tantalizing finding that invites further experimentation.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode

contemplated by the inventor of carrying out his invention.

Claims 1-8, 10, 11, 47-51, 61 and 65 also remain rejected under 35 U.S.C. § 112, first paragraph for reasons of record in the previous Office Action, paper number 11 at page 7. Since the claimed invention is not supported by either a specific, substantial and credible asserted utility of a well established utility, one skilled in the art clearly would not know how to use the claimed invention. This rejection is maintained for reasons cited above.

Claims 1-8, 10, 11, 47-51, 61 and 65 remain rejected under 35 U.S.C. § 112, first paragraph as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants argue that the disclosure that β10 is in the cysteine-knot growth factor superfamily, taken with alignments of β10 with other members of the family is sufficient to establish possession of the claimed invention. This argument has been fully considered but is not deemed persuasive because The specification does not specify what *"β10 activity"* is; it merely demonstrates one effect of β10 in a transgenic system. It remains that the activity of β10 remains largely uncharacterized, that the specification does not disclose even a single allelic variant, splice variant or naturally occurring variant, and that the only orthologs disclosed are human and mouse. It remains that there is not sufficient written description to support the breadth of the claims, which encompass "β10" from any possible species, as well as any variant of such so long as "an activity" is retained (or duplicated). It is noted that antigenicity/immunogenicity is considered to be an activity of proteins. Accordingly, the claims encompass mimotopes, so long as some portion of the DNA encoding the mimotope can hybridized to SEQ ID NO: 2 or to a sequence encoding SEQ ID NO: 1. It remains that all the disclosure provides, as argued by applicants at page 11 of the response, is a statement that the variants, orthologs, splice variants, etc. are part of the invention, and references to potential methods of isolating such. Only one specific nucleic acid is actually disclosed (it is noted that applicants allege at page 11 of their response that murine and human β10

are 93% identical, but no portion of the specification is referenced for such data). Therefore, it remains that only nucleic acids of SEQ ID NO: 2 or which encode SEQ ID NO: 1 or 3 find adequate written description in the specification as originally filed.

Claim 50 is rejected under 35 U.S.C. § 112, first paragraph as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new matter rejection.**

Claim 50 as amended recites "at least one nucleic acid molecule of Claims 1, 2 or 3". The Examiner can find no basis in the specification as originally filed for concatameric fusion proteins, see for example page 22, first full paragraph.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-8, 10, 11, 47-51, 61 and 65 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims which recite "moderately" or "highly" stringent conditions, such as claims 1-3, remain indefinite because there is no limiting definition of such in the specification, and the metes and bounds of that which will hybridize are dependent upon the conditions under which the hybridization is performed. The discussion of such at pages 31-33 of the specification is noted but vague, fails to breathe life and meaning into the term, is exemplary rather than limiting, and thus is insufficient to render the claims definite. Applicants citation of textbooks and the knowledge of one skilled in the art has been fully considered but not deemed persuasive as the terms are relative terms with no well-defined limits in the art, and therefore is not persuasive for reasons cited in the original rejection and reproduced herein.

Claim 2 remains further indefinite at part (d) of the claim, as the nature of the 'fragment of

at least 16 nucleotides' is not clear. This also applies to other claims, for example claim 3, part (f). Applicants traversal that they do not understand the rejection is noted. The rejection is on the basis that it is not clear what the "fragment of at least about 16 nucleotides" is a fragment *of*. There is no connection in the claim between said fragment and the nucleotide sequence of SEQ ID NO: 2. Accordingly, the metes and bounds of the claims cannot be determined.

Claim 3 remains further indefinite for failing to adequately point out that which applicant sees as the invention. There is no upper limit to the number of substitutions, insertions, deletions, or truncations, such that there is no requirement for any structural similarity to the disclosed nucleic acids. Applicants traversal that the specification provides 'ample disclosure to allow one skilled in the art to determine appropriate substitutions" etc. has been fully considered but is not deemed persuasive. This is not an enablement rejection, but rather a rejection under 35 U.S.C. § 112, second paragraph on the basis that the metes and bounds of the claims cannot be determined. As claim 3 has no limits on the number of changes, one of ordinary skill in the art would not be able to determine whether a given protein did or did not fall within the metes and bounds of the claim, and the claim fails to point out with particularity that which is the disclosed invention.

Claim 8 also remains further indefinite for failing to adequately point out that which applicant sees as the invention: The claim recites that it is a β10 polypeptide that is to be produced, whereas the claims from which it depends do not provide antecedent basis for the recitation of "β10 polypeptide", nor does the specification adequately breathe life and meaning into the term such that the metes and bounds of the claim can be discerned. Simply put, it is not clear what the identifying characteristics of a "β10 polypeptide" are. Applicants traversal that the specification defines β10 has been fully considered but is not deemed persuasive. As the specification definition is itself indefinite, it cannot be used to breath life and meaning into the claims. It remains that the claims from which claim 8 depends to not use the term "β10 polypeptide", so that it is not clear how such is to be produced.

Claim 61 remains indefinite as the metes and bounds of "human β10 polypeptide" are not clear. Applicants traversal of this rejection has been fully considered but is not deemed persuasive.

The cited portion of the specification does not use the term "human β10 polypeptide". Such might refer either to a β10 polypeptide isolated from a human, or alternatively to any polypeptide with similar activity to human β10, for example. As the specification does not breath life and meaning into the term, the claim is indefinite.

The remaining claims are rejected for depending from an indefinite claim.

Rejections Over Prior Art:

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-5, 7 and 11 remain rejected under 35 U.S.C. 102(b) as being anticipated by, or in

the alternative under 35 U.S.C. § 103(a) as being obvious over G.G. Mahairas et al., Locus AQ495547 disclosed 4/28/99 for reasons of record in the previous Office Action.

Applicants traversal has been fully considered but is not deemed persuasive. Applicants argue that Mahairas' disclosure is not enabling. This argument has been fully considered but is not deemed persuasive because the mere disclosure of a DNA sequence enables one of ordinary skill in the art to make it. It is not necessary that Mahairas have appreciated the particular properties of the sequence, it is sufficient that the sequence meets the structural and functional requirements of the claims. Applicants have provided neither argument, facts or evidence that the DNA of Mahairas is not anticipatory nor would render obvious the claimed invention. Applicants argument that the claims do not recite the term "antibody-binding epitope" has been fully considered but is not deemed persuasive. The claims require "an activity" of the human $\alpha 2/\beta 10$ heterodimer. As antibody binding is "an activity", the fact that the protein encoded by Mahairas' DNA would comprise an antibody binding epitope is sufficient to meet the functional limitation. Applicants are reminded that the Examiner is required to give the claims their broadest reasonable interpretation when applying the prior art.

Claims 6, 8, and 48-50 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Mahairas et al., locus AQ495547, as cited above, in view of Sibson et al., WO94/01548.

Applicants traverse that there is no motivation to apply the teachings of Sibson to the DNA of Mahairas et al. This argument has been fully considered but is not deemed persuasive because as stated in the previous Office Action, Sibson et al. disclose that it is generally useful to place a desired cDNA sequence into an expression vector, host cell, and express the encoded protein, as well as to raise antibodies to proteins encoded by such cDNA's. See pages 8-13. Expression in eukaryotic cells, and the advantages thereof, are discussed at page 9, first paragraph. Fusion proteins are also taught, see page 11, lines 15-15 and 26-29. As Sibson is directed to DNAs such as that disclosed by Mahairas, which are obtained by cDNA cloning, the person of ordinary skill in the art at the time the invention was made would have been motivated to use the DNA's disclosed by the primary

reference to express and then isolate the encoded polypeptide using a heterologous promoter, to make a fusion protein of such, and to express such in eukaryotic cells, using a viral vector, all as taught by Sibson et al. in view of Sibson et al.'s suggestion that it would be desirable to do so, as cited above.

Advisory Information:

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Lorraine M. Spector, whose telephone number is (703) 308-1793. Dr. Spector can normally be reached Monday through Friday, 9:00 A.M. to 5:30 P.M.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr. Gary L. Kunz, at (703)308-4623.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist at telephone number (703) 308-0196.

Certain papers related to this application may be submitted to Group 1800 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Official papers filed by fax should be directed to (703) 872-9306 (before final rejection) or (703)872-9307 (after

final). Faxed draft or informal communications with the examiner should be directed to (703) 746-5228.

Lorraine Spector, Ph.D.
Primary Examiner

LMS
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